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EXAMINER	
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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/054,638	RYALL, ROBERT P.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicant's Amendment

1) Acknowledgment is made of Applicant's amendment filed 03/04/09 in response to the non-final Office Action mailed 09/04/08.

Status of Claims

2) Claim 18 has been amended via the amendment filed 03/04/09.

Claims 19-36, 46 and 48-51 have been canceled via the amendment filed 03/04/09.

Claim 18 is pending and is under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The provisional rejection of claims 19-33 made in paragraph 15 of the Office Action mailed 12/12/07 and maintained in paragraph 13 of the of the Office Action mailed 09/04/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is moot in light of Applicant's cancellation of the claims.

6) The rejection of claims 19-36, 46 and 48-51 made in paragraph 15 of the Office Action mailed 09/04/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is moot in light of Applicant's cancellation of the claims.

7) The rejection of claims 19-22, 24-29, 31 and 32 made in paragraph 17 of the Office Action mailed 09/04/08 under 35 U.S.C. § 102(b) as being anticipated by Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983), is moot in light of Applicant's cancellation of the claims.

8) The rejection of claims 34-36, 46 and 48 made in paragraph 19 of the Office Action mailed 09/04/08 under 35 U.S.C § 103(a) as being unpatentable over Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983) as applied to claim 18 above, and further in view of Fusco *et al.* (*Expert Opin. Investig. Drugs* 7: 245-252, 1998), is moot in light of Applicant's cancellation of the claims.

9) The rejection of claim 33 made in paragraph 20 of the Office Action mailed 09/04/08 under 35 U.S.C § 103(a) as being unpatentable over Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983, of record) as applied to claim 18, and McMaster (US 6,146,902, of record) and further in view of Perkins BA (*JAMA* 283: 2842-2843, 07 June 2000, of record), is moot in light of Applicant's cancellation of the claim.

Applicant's state that the rejection is moot in view of the cancellation made herein for other reasons unrelated to patentability. No rebuttal to this statement is in order.

10) The rejection of claim 51 made in paragraph 21 of the Office Action mailed 09/04/08 under 35 U.S.C § 103(a) as being unpatentable over Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983) as applied to claims 33 and 18 above, and further in view of McMaster (US 6,146,902), is moot in light of Applicant's cancellation of the claim.

11) The rejection of claims 49 and 50 made in paragraph 22 of the Office Action mailed 09/04/08 under 35 U.S.C § 103(a) as being unpatentable over Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983) as modified by Fusco *et al.* (*Expert Opin. Investig. Drugs* 7: 245-252, 1998) as applied to claim 48 above, and further in view of Costantino *et al.* (*Vaccine* 10: 691-698, 1992), is moot in light of Applicant's cancellation of the claims.

Applicant's statement(s) made with regard to the art rejections of record has been considered, but is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

12) The provisional rejection of claim 18 made in paragraph 15 of the Office Action mailed 12/12/07 and maintained in paragraph 13 of the of the Office Action mailed 09/04/08 under the judicially created doctrine of obviousness-type double patenting over claim 56 of the co-pending application 11232160, is withdrawn in light of the current abandoned status of the co-pending application 11232160.

13) The rejection of claim 18 made in paragraph 15 of the Office Action mailed 09/04/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claim 18 made in paragraph 17 of the Office Action mailed 09/04/08 under 35 U.S.C. § 102(b) as being anticipated by Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983, of record), is withdrawn in light of Applicants' amendment to the claim.

Applicant's statement(s) made with regard to this art rejection has been considered, but is moot in light of Applicants' amendment to the claim.

All of Applicant's previous arguments on the obviousness rejection(s) that were set forth previously have been fully addressed by the Office previously. See for example paragraph 14 of the Office Action mailed 09/04/08.

New Rejection(s) Necessitated by Applicant's Amendment

Rejection(s) Under 35 U.S.C. § 112, First Paragraph (New Matter)

15) Claim 18 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 18, as amended, is now drawn to an immunological composition comprising a combination of four distinct and separately made protein-capsular polysaccharide conjugates, wherein the first conjugate comprises purified *N. meningitidis* capsular polysaccharide of serogroup W-135 conjugated to a carrier protein, wherein the second conjugate comprises purified *N. meningitidis* capsular polysaccharide of serogroup Y conjugated to a carrier protein, the third conjugate comprises purified *N. meningitidis* capsular polysaccharide of serogroup A conjugated to a carrier protein, and the fourth conjugate comprises purified *N. meningitidis* capsular polysaccharide of serogroup C conjugated to a carrier protein, wherein said immunological composition is capable of eliciting an immune response in a human to each of said polysaccharides. Applicant does not specifically point to one or more parts of the specification where support can be found for the claimed composition. The 'immune response in a human to each of said polysaccharides' elicited by the composition as claimed encompasses within its

scope cellular immune response, local or secretory immune response, serum IgM, IgA and IgG immune responses to each of the four capsular polysaccharides of *N. meningitidis* serogroups W-135, Y, A and C. However, an immunological composition capable of eliciting such a broad immune response lacks descriptive support in the as-filed specification. A review of the specification indicates that the only tetravalent conjugate composition that is supported in the as-filed specification is the one comprising separately made purified *N. meningitidis* capsular polysaccharides of serogroups W-135, Y, A and C conjugated to a carrier protein, wherein the tetravalent conjugate --elicits a serum IgG response and a serum bactericidal antibody response in a human to each of the capsular polysaccharides--.

Applicant is invited to point to specific line and page numbers of the specification, as originally filed, that provide descriptive support for the immunological composition of the now claimed scope, or alternatively to remove the new matter from the claim(s). Applicant should specifically point out the support for any amendments made to the claim. See MPEP 714.02 and 2163.06.

Rejection(s) Under 35 U.S.C. § 112, Second Paragraph

16) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

17) Claim 18 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 18, as amended, has improper antecedent basis in the limitation: 'the purified …. polysaccharide'. See lines 3, 5, 6 and 8. For the purpose of distinctly claiming the subject matter, it is suggested that Applicant replace the above-identified limitation with the limitation --purified ….. polysaccharide--.

Rejection(s) under 35 U.S.C. § 103

18) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior

art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

19) Claim 18 is rejected under 35 U.S.C § 103(a) as being unpatentable over Beuvery *et al.* (*Infect. Immun.* 41: 609-617, 1983, of record) in view of McMaster (US 6,146,902, of record), Perkins BA (*JAMA* 283: 2842-2843, 07 June 2000, of record) and Cadoz *et al.* (*Vaccine* 3: 340-342, 1985, abstract).

It is noted that a conjugate of meningococcal serogroup B capsular polysaccharide is not a required element of the instantly claimed immunological composition.

Beuvery *et al.* taught an immunogenic vaccine composition (i.e., immunological composition) comprising a mixture of individually made conjugates (i.e., first, second, third, and fourth conjugates) of purified capsular polysaccharides of four different meningococcal serogroups A, C, W-135 and Z, wherein each of the purified capsular polysaccharide is individually conjugated to the protein carrier, tetanus toxoid. The prior art liquid composition was used to immunize mice. See paragraph bridging pages 613 and 614; 'Materials and Methods'; Table 5; and seventh full paragraph on page 615. After injection of a mixture of four distinct, individually made polysaccharide-tetanus toxoid conjugates, including the group C polysaccharide conjugate, Beuvery *et al.* reported no antigenic (intermolecular) competition in the anti-polysaccharide and anti-tetanus toxoid response, even though the same carrier protein was used.

The teachings of Beuvery *et al.* are explained above, which do not expressly teach that their combined conjugate vaccine composition comprises a capsular polysaccharide-carrier protein conjugate of serogroup Y *N. meningitidis*.

However, individually produced meningococcal serogroup Y capsular polysaccharide-protein conjugate vaccine was already known in the art at the time of the instant invention. For example, McMaster disclosed an individually made purified meningococcal Y capsular polysaccharide-protein carrier conjugate vaccine and provided detailed teachings as to how to successfully make the individual purified meningococcal Y capsular polysaccharide-protein carrier conjugates in addition to making purified meningococcal A, C and W-135 capsular polysaccharide-protein carrier conjugates. McMaster disclosed a vaccine or immunological composition comprising a sterile liquid solution of individual capsular polysaccharide-protein conjugates comprising purified capsular polysaccharides of *Neisseria meningitidis* belonging to the serogroup A, C, W-135 and Y conjugated to diphtheria toxoid protein for human or animal use. Column 7; Table 3; lines 59-64 of column 3; paragraph bridging columns 3 and 4; and lines 3-6 in column 4. The serogroup Y meningococcal capsular polysaccharide conjugate is identified by the lot number D01880. See Table 3. The production of meningococcal serogroup A, C, Y and W-135 conjugates are described in columns 6 and 7; and Example 1.

Perkins expressly included meningococcal serogroups A, C, Y and W-135 in the list of globally most important causes of meningococcal disease. See third full paragraph on page 2842. Perkins taught that because of the variation in serogroup distribution by region and age and potential for capsular switching, there is an identified need for development and availability of *multivalent* meningococcal conjugates, with all of meningococcal serogroups A, C, Y and W-135, as stand-alone vaccines and in combination with other vaccines. Perkins expressly suggested the inclusion of A, C, Y and W-135 serogroups in conjugate meningococcal vaccines as the broadest approach based on the current understanding of *N. meningitidis*. See last two full paragraphs on page 2843.

Cadoz *et al*. demonstrated that a tetravalent vaccine comprising capsular polysaccharides of serogroups A, C, Y and W-135 of *N. meningitidis* was immunogenic without conjugation to a carrier protein and induced a four-fold increase in bactericidal titers in humans immunized therewith to all the four capsular polysaccharides. See abstract.

With the concept of providing multiple meningococcal serogroup capsular polysaccharide-protein conjugates in a multivalent immunogenic formulation already known in the art as demonstrated by Beuvery *et al*., and given that individually produced purified meningococcal

serogroup Y capsular polysaccharide-protein conjugate was already known in the art as taught by McMaster, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine McMaster's individually produced, sterile, purified meningococcal serogroup Y capsular polysaccharide-protein conjugate with Beuvery's vaccine composition comprising a mixture of conjugates of purified capsular polysaccharides of four different meningococcal serogroups, A, C, W-135 and Z to produce the composition of the instant invention. With the identified need in the art for development and availability of *multivalent* meningococcal conjugates with all of meningococcal serogroups A, C, Y and W-135 as stand-alone vaccines and in combination with other available vaccines as expressly taught by Perkins, and with the reasonable expectation of success already demonstrated in the art with a multivalent meningococcal conjugate vaccine by Beuvery *et al.*, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent, broadest approach-based, stand-alone combination meningococcal capsular polysaccharide conjugate composition of serogroups A, C, Y and W-135 that addresses the variation in serogroup distribution by region and age and the potential for capsular switching, as taught by Perkins. Beuvery's vaccine composition as modified by McMaster and Perkins would be expected to elicit at least an IgM response to each of the capsular polysaccharides in a human subject since each of the serogroup A, C, Y and W-135 meningococcal capsular polysaccharides were known in the art to be immunogenic in humans even without conjugation to a carrier protein as taught by Cadoz *et al.*

Claim 18 is *prima facie* obvious over the prior art of record.

Relevant Prior Art

20) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicant's disclosure:

- Fusco *et al.* (*Expert Opin. Investig. Drugs* 7: 245-252, 1998, of record) taught a trivalent combination vaccine comprising individual meningococcal serogroup A, B and C conjugates. The trivalent conjugate vaccine was shown to be safe and highly immunogenic in mice and non-human primates, *generating CPS-specific bactericidal antibodies to each of the three major serogroups of meningococci*. Fusco *et al.* taught that this trivalent conjugate vaccine

would be expected to provide world-wide protection against meningococcal disease. See abstract. Thus, the concept of combining two or more individually produced meningococcal capsular polysaccharide-protein conjugates in a multivalent conjugate formulation that elicited bactericidal antibodies to each of the serogroup capsular polysaccharides including the serogroup B capsular polysaccharide in mice and non-human primates was already known in the art. Fusco *et al.* already established reasonable expectation of success of combining three different meningococcal serogroup capsular polysaccharide-protein conjugates including the poorly immunogenic serogroup B capsular polysaccharide to produce an immunogenic combination conjugate vaccine that generated *CPS-specific bactericidal antibodies to each of the three major serogroups of meningococci*. Fusco's studies indicate total lack of unpredictability and lack of carrier-induced epitopic suppression associated with such a combination meningococcal vaccine. See entire document. Fusco *et al.* clearly demonstrated the lack of unpredictability and provided a showing of complete success with regard to the immunogenicity of the multivalent meningococcal capsular polysaccharide-protein conjugate vaccines.

- Tai *et al.* (*Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al*. September 8-13, Baltimore, USA, pages 214-215, 1996, of record) taught a multivalent combination vaccine comprising individual meningococcal serogroup A, B and C conjugates and its preclinical evaluation in monkeys. The combination conjugate vaccine elicited *bactericidal antibodies to capsular polysaccharides of all the three meningococcal serogroups* after only one injection of the multivalent formulation. Thus, the concept of combining multiple individually produced meningococcal capsular polysaccharide-protein conjugates in a multivalent conjugate formulation that elicited bactericidal antibodies to each of the serogroup capsular polysaccharides including the serogroup B capsular polysaccharide in monkeys immunized therewith was already known in the art. Tai *et al.* thus established a reasonable expectation of success of combining multiple different meningococcal serogroup capsular polysaccharide-protein conjugates including the supposedly poorly immunogenic serogroup B capsular polysaccharide to produce an immunogenic combination conjugate vaccine and *reported no unpredictability and no indication of carrier-induced epitopic suppression* associated with such a combination meningococcal vaccine. See pages 214 and 215.

Remarks

21) Claim 18 stands rejected.

22) Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS
from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

23) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

24) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

25) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on

Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

June, 2009